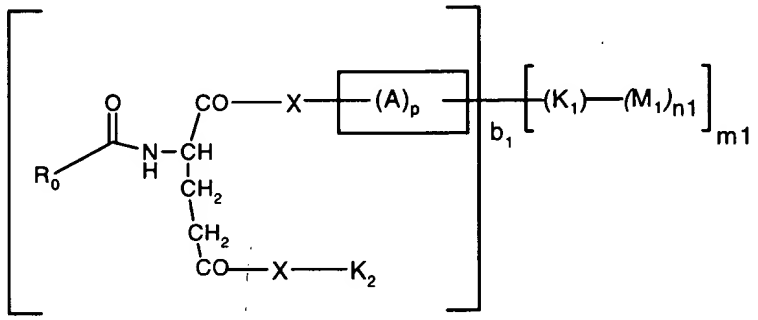
IN THE CLAIMS

Please cancel claims 1-15, 18-20, 22-25, 27, 42-80, and 83-127.

Please amend the following claims as shown.

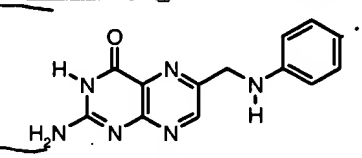
--16. (Amended) [The composition of claim 11] A diagnostic, therapeutic or radiotherapeutic or chemotherapeutic composition for visualization, therapy, chemotherapy or radiotherapy of tissues or organs that overexpress folate-binding protein comprising:

a) a folate-receptor binding ligand comprising one or more folate-receptor binding moieties, at least one of which is conjugated through its alpha carboxylate via an optional linking group to one or more macrocyclic or non-macrocyclic metal-chelating ligand radicals that are optionally chelated to paramagnetic, superparamagnetic, radioactive or non-radioactive metals for detection outside the body by imaging means for diagnosis or for providing a therapeutic, chemotherapeutic, or radiotherapeutic effect; wherein said folate receptor binding ligand has the structure of formula **II**:

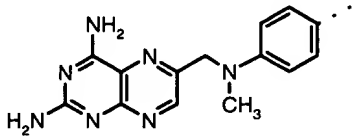


II

wherein R_0 is a folate-receptor binding residue of formula:



or



each X is independently -O-, -S-, -NH-, or -NR_1-;
n1 is 0 or 1;
b1 is 1 to 3;
m1 is 1 to 81;
each K_1 is independently

a) a macrocyclic or non-macrocyclic metal-chelating ligand radical that is optionally chelated to a paramagnetic, superparamagnetic, radioactive

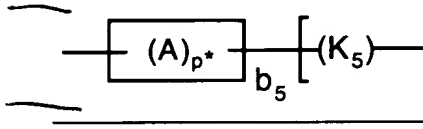
or non-radioactive metal M_1,

or

b) a chemotherapeutic drug;

$-K_2$ is -H, -alkyl, -alkenyl, -alkynyl, -alkoxy, -aryl, -alkyl, $-CON(R_2)_2$, -glutamate, -polyglutamate, or $-K_3$;

$-K_3$ is



;

wherein

$-K_5$ is either

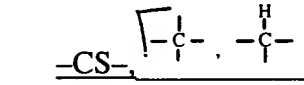
a) a macrocyclic or non-macrocyclic metal-chelating ligand that is optionally chelated to a paramagnetic, superparamagnetic, radioactive or non-radioactive metal M_5, or

b) a chemotherapeutic drug

n5 is 0 or 1;

b5 is 1 to 3;

m5 is 1 to 81;

-(A)p- and –(A)p*- are each independently optional linkers comprising a straight or branched chain wherein the moieties "A" are the same or different and selected from the group consisting of: $-CH_2-$, $-CHR_3-$, $-CR_4R_5-$, –CH=CH–, $-CH=CR_6-$, $>CR_7-CR_8<$, -C=C-, $-CR_9=CR_{10}-$, -C≡C–, -cycloalkylidene-, -cycloalkenyl-, -arylidene-, -heterocyclo-, carbonyl (-CO-), -O-, -S-, –NH–, –HC=N–, $-CR_{11}=N-$, $-NR_{12}-$, –CS–,  , and

p and p* are independently 0 to 24,

or –X-[(A)]p- and –X-[(A)p]*- may each independently be the group –Q- wherein -Q– is $-[C(R')(R'')]_{s1}-[C(t)(R_{21})]_{s2}-[C(R_{22})(R_{23})]_{s3}$-X3-Y-X4-;

wherein

each s1, s2, s3, and s4 is independently 0 to 2;

each X3, X4, X5, and X6 is independently a single bond, –O-, -S-, or $-N(R_{24})-$;

Y is a single bond, $-C(R_{25})(R_{26})-$, or Y1 wherein,

Y1 is –C(=X5)-X6-W-, wherein

W is a single bond, -alkylidene-, -cycloalkylidene-, -arylidene-, -alkenylidene-, or –alkynylidene-, whose carbon atoms may or may not be substituted;

t is H, R_{27}, $-C(O)OR_{28}$, $-P(O)(OR_{29}))OH$, $-P(O)(OR_{30}))OR_{31}$, $-P(O)(OR_{32})R_{33}$, $-P(O)(OH)R_{34}$, $-C(O)N(R_{35})(R_{36})$, or $C(O)NH(R_{37})$;

each R' and R" is independently a single bond, H, alkyl, alkoxy, cycloalkyl,

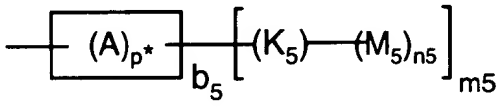
hydroxyalkyl, aryl, or heterocyclo, each of which is optionally substituted,

each R_3 through R_5, R_7, R_8, R_{21} through R_{23}, and R_{25} through R_{27} is independently H, alkyl, alkoxy, halogen, hydroxy, cycloalkyl, hydroxyalkyl, aryl, or heterocyclo, each of which is optionally substituted;

each R_1, R_2, R_6, R_9 through R_{12}, R_{24}, and R_{28} through R_{37} is independently H, alkyl, alkenyl, cycloalkyl, aryl, a 5- or 6-membered nitrogen or oxygen containing heterocycle;

wherein

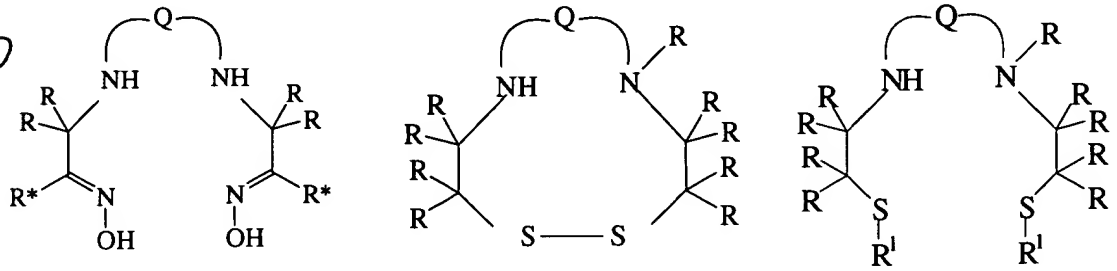
$-K_2$ is



;

and both $-K_1$ and $-K_5$ are macrocyclic or non-macrocyclic metal chelates that are each optionally chelated to radioactive, nonradioactive, paramagnetic or superparamagnetic metals M_1 or M_5;

wherein - $[(A)p]-K_1$ and $-[(A)p^*]-K_5$ are each in their entirety, polydentate ligands radicals of formula **IIIa - IIIc**:



IIIa **IIIb** **IIIc**

wherein

Q is the group $-(C(RR))_{m1}-Y^1(C(RR))_{m2}-(Y^2-(C(RR))_{m3})_n-$,

wherein

Y^1 and Y^2 are independently $-CH_2-$, -NR-, -O-, -S-, -SO-, $-SO_2-$ or -Se-;

n is 0 or 1; and m1, m2 and m3 are integers independently selected from 0 to 4, provided that the sum of m1 and m2 is greater than zero;

all R and R* groups are independently $-R^4$, -Cl, -F, -Br, $-OR^5$, $-COOR^5$, $-CON(R^5)_2$, $-N(R^5)_2$, $-alkyl-COOR^5$, $-alkyl-C(O)-N(R^5)_2$; $-alkyl-N(R^5)_2$; $-C(O)OR^5$; $-C(O)N(R^5)_2$; $-aryl-N(R^5)_2$; acyl; acyloxy; heterocyclo; hydroxyalkyl; $-SO_2-R^5$; $-alkyl-SO_2-R^5$; or $-R^3$;

wherein

each $-[R^3]-$ is, in its entirety, the linking group $-[(A)p]-$ or $-[(A)p^*]-$ that serves to couple the metal chelating ligand radical to –X-;

each $-R^4$ is independently -H, -alkyl, -alkoxy, -hydroxy, -cycloalkyl, -

cont A1

hydroxyalkyl, -aryl, or -heterocyclo, each of which is optionally substituted;
each $-R^5$ is independently -H, -alkyl, -aryl, -cycloalkyl or -hydroxyalkyl, each of which is independently substituted;

with the provisos that a carbon atom bearing an R group is not directly bonded to more than one heteroatom; and
at least one R or R* group on each $-K_1$ and $-K_5$ is $-[R^3]-$;

or a pharmaceutically acceptable salt thereof; in a pharmaceutically acceptable carier.--

In claim 17, line 1, delete "claim 11" and replace it with --claim 16--.

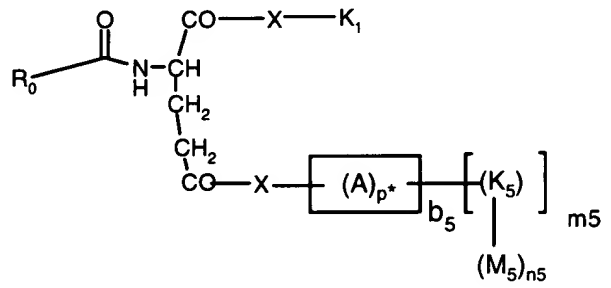
--~~21~~ 3. (Amended) [The compositions of claim 18] A diagnostic, therapeutic or radiotherapeutic composition for visualization, therapy or radiotherapy of tissues or organs that overexpress folate-binding protein using nuclear medicine, magnetic resonance imaging or neutron capture radiotherapy applications comprising:

a) a folate-receptor binding ligand and
b) a pharmaceutically acceptable carrier

wherein said folate-receptor binding ligand has the structure of formula **IIb**:

A2

T, 1040

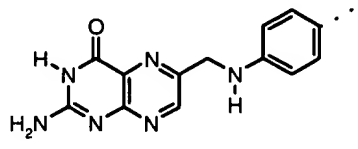


IIb

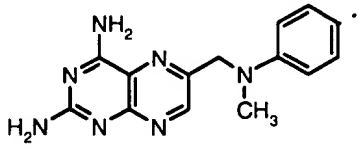
wherein

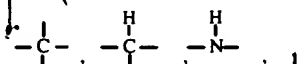
$-K_1$ is –H, -alkyl, -alkenyl, -alkynyl, -alkoxy, -aryl, -alkyl, $-CON(R_2)_2$, -glutamate, or –polyglutamate;
$-K_5$ is a polydentate metal chelating ligand;
M_5 is a radioactive, paramagnetic or superparamagnetic metal;
each –X- is independently –O-, -S-, -NH-, or $-NR_1-$;
b5 = 1 to 3, m5 = 1; n5 is 0 or 1;
$-R_0$ is a folate-receptor binding residue of formula:

T, 1041



or



each –[(A)p*]- is an optional linker independently comprising a straight or branched chain made up of "p*" individual (A) moieties that are the same or different and are selected from the group consisting of: $-CH_2-$, $-CHR_3-$, $-CR_4R_5-$, $-CH=CH-$, $-CH=CR_6-$, $>CR_7-CR_8<$, $>C=C<$, $-CR_9=CR_{10}-$, -C≡C–, -cycloalkylidene-, -cycloalkenyl-, -arylidene-, -heterocyclo-, carbonyl (-CO-), -O-, -S-, –NH–, –HC=N–, $-CR_{11}=N-$, $-NR_{12}-$, –CS–, and  ; and p* is 0 to 24;

or –X-[(A)]p*- is, in its entirety, the group –Q-

wherein

-Q– is $-[C(R')(R'')]_{s1}-[C(t)(R_{21})]_{s2}-[C(R_{22})(R_{23})]_{s3}$-X3-Y-X4-;

wherein

s1, s2, s3, and s4 are independently 0 to 2;

X3, X4, X5, and X6 are independently a single bond, –O-, -S-, or $-N(R_{24})-$;

Y is a single bond, $-C(R_{25})(R_{26})-$, or -Y1-

wherein,

Y1 is –C(=X5)-X6-W-, wherein

W is a single bond, -alkylidene-, -cycloalkylidene-, -arylidene-, -alkenylidene-, or –alkynylidene-, whose carbon atoms are optionally substituted;

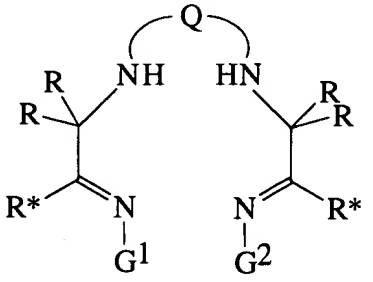
t is H, R_{27}, $-C(O)OR_{28}$, $-P(O)(OR_{29}))OH$, $-P(O)(OR_{30}))OR_{31}$, $-P(O)(OR_{32})R_{33}$, $-P(O)(OH)R_{34}$ $-C(O)N(R_{35})(R_{36})$, or $C(O)NH(R_{37})$;

each -R' and -R" is independently a single bond, -H, -alkyl, -alkoxy, -cycloalkyl, -hydroxyalkyl, -aryl, or -heterocyclo, each of which is optionally substituted,

each $-R_3$ through $-R_5$, $-R_7$, $-R_8$, $-R_{21}$ through $-R_{23}$, and $-R_{25}$ through $-R_{27}$ is independently -H, -alkyl, -alkoxy, -halogen, -hydroxy, -cycloalkyl, -hydroxyalkyl, -aryl, or -heterocyclo, each of which is optionally substituted;

each $-R_1$, $-R_2$, $-R_6$, $-R_9$ through $-R_{12}$, $-R_{24}$, and $-R_{28}$ through $-R_{37}$ is independently -H, -alkyl, -alkenyl, -cycloalkyl, -aryl, or a 5- or 6-membered nitrogen or oxygen containing heterocycle;

wherein $-K_5$ is a polydentate metal-chelating ligand radical of formula **V**:



V

wherein

Q is the group $-(C(RR))_{m1}-(Y^1)_n-(C(RR))_{m2}-(Y^2-(C(RR))_{m3})_{n1}$;

Y^1 and Y^2 are each independently $-CH_2-$, -NR-, -O-, -S-, -SO-, $-SO_2-$ or -Se-;

n and n1 are each independently 0 or 1; and m1, m2 and m3 are independently 0 or an integer from 1 to 4; provided that m1 and m2 are not both 0, that m1 + m2 + n +n1 is less than 6 and that a carbon atom bearing an R group is not directly bonded to more than one heteroatom;

each R and R* group is independently: -H, $-R^4$; -alkoxy; -hydroxy; -halogen, [especially fluoro,] -haloalkyl, $-OR^5$, $-C(O)-R^5$, $-C(O)-N(R^5)_2$, $-N(R^5)_2$, $-N(R^5)-COR^5$, -alkyl-$C(O)-OR^5$, -alkyl-$C(O)-N(R^5)_2$, -alkyl-$N(R^5)_2$-, -alkyl-$N(R^5)-COR^5$, -aryl-$C(O)-OR^5$, -aryl-$C(O)-N(R^5)_2$, aryl-$N(R^5)_2$-, -aryl-$N(R^5)-COR^5$, -nitrile, -acyl, -acyloxy, -heterocyclo, -hydroxyalkyl, -alkoxyalkyl, -hydroxyaryl, -arylalkyl, $-SO_2-R^5$, -alkyl-SO_2-R^5, or $-[R^3]-$;

wherein

each $-[R^3]-$ is, in its entirety, the linking group $-[(A)p^*]-$ that serves to couple the metal chelating ligand radical $-K_5$ to –X-;

each $-R^4$ is independently -H, -alkyl, -alkoxy, -hydroxy, -cycloalkyl, -hydroxyalkyl, -aryl, or -heterocyclo, each of which is optionally substituted;

each $-R^5$ is independently -H, -alkyl, -aryl, -cycloalkyl or -hydroxyalkyl, each of which is independently substituted;

or

two R groups, or an R group and an R* group, taken together with the one or more atoms to which they are bonded, form a saturated or unsaturated, spiro or fused, carbocyclic [(such as fused 1,2-phenyl)] or heterocyclic ring which [may be unsubstituted or] <u>is optionally</u> substituted by one or more groups R or R* groups above;

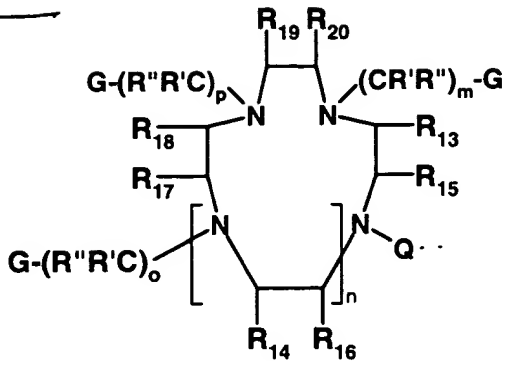
each $-G^1$ and $-G^2$ is independently -OH or $-(NR^6)_2$; with the proviso that at least one of $-G^1$ or $-G^2$ is $-(NR^6)_2$, where each $-R^6$ is independently -hydrogen, -alkyl, -aryl, -acyl or $-[R^3]-$; and

A is a linking group; and p is 0 or a positive integer;

with the proviso that at one to three -R , -R*, or $-R^6$ groups is $-[R^3]-$;

or a pharmaceutically acceptable salt thereof.--

~~126~~ 4. (Amended) The composition of claim [18] ~~21~~ 3 wherein M_1 or both M_1 and M_5 are paramagnetic or superparamagnetic metals and K_1 or both $-K_1$ and $-K_5$ are enhanced relaxivity polyaza macrocyclic radicals of formula **VI**:



VI

wherein

n is 0 or 1;

each m, o, and p is independently 1 or 2;

Q is $-[C(R')(R'')]_{s1}-[C(t)(R_{21})]_{s2}-[C(R_{22})(R_{23})]_{s3}$-X3-Y-X4-;

wherein

s1, s2, s3, and s4 are independently 0 to 2;

Y is a single bond, $-C(R_{25})(R_{26})$-, or Y1 wherein,

Y1 is –C(=X5)-X6-W-, wherein

W is a single bond, -alkylidene-, -cycloalkylidene-, -arylidene-, -alkenylidene-, or –alkynylidene-, whose carbon atoms [may or may not be] <u>are optionally</u> substituted;

t is H, R_{27}, $-C(O)OR_{28}$, $-P(O)(OR_{29}))OH$, $-P(O)(OR_{30}))OR_{31}$, $-P(O)(OR_{32})R_{33}$, $-P(O)(OH)R_{34}$ $-C(O)N(R_{35})(R_{36})$, or $C(O)NH(R_{37})$;

each G is independently -C(O)OR'", -P(O)(OR'")OH, $-P(O)(OR'")_2$, -P(O)(OR'")R", -P(O)(OH)R" $C(O)N(R'")_2$, or C(O)NH(R'");

each -R' and -R" is independently a single bond, -H, -alkyl, -alkoxy, -cycloalkyl, hydroxyalkyl, -aryl, or -heterocyclo, each of which is optionally substituted,

each -R'" is independently a -H, -alkyl, -cycloalkyl, -hydroxyalkyl, -aryl, or -heterocyclo, each of which is optionally substituted,

each $-R_{13}$ through $-R_{23}$, and $-R_{25}$ through $-R_{27}$ is independently -H, -alkyl, -alkoxy, -halogen, -hydroxy, -cycloalkyl, -hydroxyalkyl, aryl, or -heterocyclo, each of which is optionally substituted;

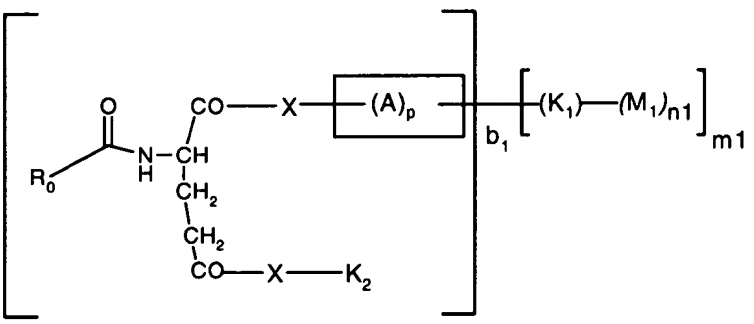
each $-R_{24}$, and $-R_{28}$ through $-R_{37}$ is independently -H, -alkyl, -alkenyl, -cycloalkyl, -aryl, a 5- or 6-membered nitrogen or oxygen containing heterocycle, each of which is optionally substituted;

or R_{13} together with R_{15}, and R_{17} together with R_{18}, independently form, together with the carbon atoms in the polyazamacrocycle to which they are attached, a fused fully or partially saturated non-aromatic cyclohexyl ring which [may be unsubstituted or] <u>are optionally</u> substituted by one or more halogen, alkyl, ether, hydroxy, or hydroxyalkyl groups, and which [may be further] <u>are optionally</u> fused to a carbocyclic ring, or R_{13} and R_{15} are each hydrogen and R_{17}, together with

R_{18}, forms a fused fully or partially saturated non-aromatic cyclohexyl ring as defined above, or R_{13}, together with R_{15}, forms a fused fully or partially saturated non-aromatic cyclohexyl ring as defined above, and R_{17} and R_{18} are hydrogen;

or a pharmaceutically acceptable salt thereof.--

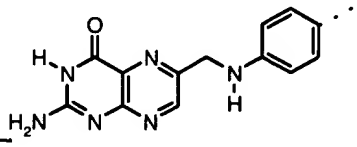
--28. (Amended) A conjugatable polyaza macrocyclic intermediate useful for the preparation of a composition [of claim 27,] for visualization or radiotherapy of tissues or organs that overexpress folate-binding protein using magnetic resonance imaging or neutron capture therapy techniques comprising one or more folate-receptor binding residues conjugated to one or more enhanced relaxivity polyaza macrocyclic radicals which are optionally chelated to a paramagnetic or superparamagnetic metal capable of either being detected outside the body by imaging means for diagnosis or capable of providing a radiotherapeutic effect using neutron capture therapy; wherein said folate-receptor binding compound has the structure of formula **IIc**:



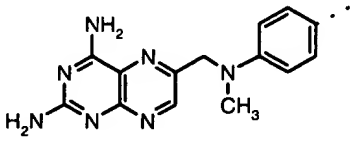
IIc

wherein

R_0 is a folate-receptor binding moietyof formula:



or



each X is independently -O-, -S-, -NH-, or -NR_1-;

n1 and n5 are independently 0 or 1;

b1 and b5 are independently 1 to 3;

m1 and m5 are independently 1 to 81;

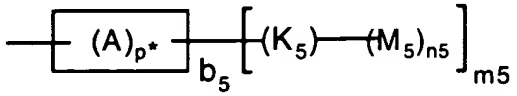
each -K_1 is independently

-H, -alkyl, -alkenyl, -alkynyl, -alkoxy, -aryl, -alkyl, -$CON(R_2)_2$, -glutamate, -polyglutamate, or –K_4;

each -K_2 is independently

-H, -alkyl, -alkenyl, -alkynyl, -alkoxy, -aryl, -alkyl, -$CON(R_2)_2$, -glutamate, -polyglutamate, or $-K_3$;

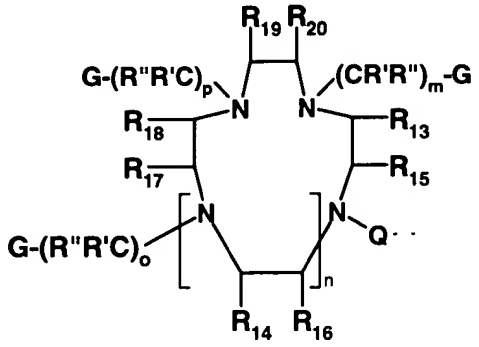
$-K_3$ is



;

M_1 and M_5 are paramagnetic or superparamagnetic metals; and

$-K_4$ and $-K_5$ are each independently enhanced-relaxivity polyaza macrocyclic metal-chelating ligand radicals of formula **VI** that are optionally chelated to M_1 and M_5:



VI

wherein

n is 0 or 1;

each m, o, and p is independently 1 or 2;

Q is $-[C(R')(R'')]_{s1}-[C(t)(R_{21})]_{s2}--[C(R_{22})(R_{23})]_{s3}$-X3-Y-X4-; wherein

s1, s2, s3, and s4 are independently 0 to 2;

X3, X4, X5, and X6 are independently a single bond, –O-, -S-, or –$N(R_{24})$-;

Y is a single bond, $-C(R_{25})(R_{26})$-, or Y1,

wherein Y1 is –C(=X5)-X6-W-,

wherein

W is a single bond, -alkylidene-, -cycloalkylidene-, -arylidene-, -alkenylidene-, or –alkynylidene-, whose carbon atoms are optionally substituted;

t is H, R_{27}, $-C(O)OR_{28}$, $-P(O)(OR_{29}))OH$, $-P(O)(OR_{30}))OR_{31}$, $-P(O)(OR_{32})R_{33}$, $-P(O)(OH)R_{34}$ $-C(O)N(R_{35})(R_{36})$, or $C(O)NH(R_{37})$;

each G is independently -C(O)OR'", -P(O)(OR'")OH, $-P(O)(OR'")_2$, -P(O)(OR'")R", -P(O)(OH)R" $C(O)N(R'")_2$, or C(O)NH(R'");

each R' and R" is independently a single bond, -H, -alkyl, -alkoxy, -cycloalkyl, -hydroxyalkyl, -aryl, or -heterocyclo, each of which is optionally substituted,

each R'" is independently -H, -alkyl, -cycloalkyl, -hydroxyalkyl, -aryl, or -

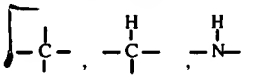
heterocyclo, each of which is optionally substituted,

each -R_{13} through -R_{23}, and –R_{25} through –R_{27} is independently -H, -alkyl, -alkoxy, -halogen, -hydroxy, -cycloalkyl, -hydroxyalkyl, -aryl, or -heterocyclo, each of which is optionally substituted;

each -R_{24}, and -R_{28} through -R_{37} is independently -H, -alkyl, -alkenyl, -cycloalkyl, -aryl, a 5- or 6-membered nitrogen or oxygen containing heterocycle, each of which is optionally substituted;

or R_{13} together with R_{15}, and R_{17} together with R_{18}, independently form, together with the carbon atoms in the polyazamacrocycle to which they are attached, a fused fully or partially saturated non-aromatic cyclohexyl ring which may be unsubstituted or substituted by one or more halogen, alkyl, ether, hydroxy, or hydroxyalkyl groups, and which may be further fused to a carbocyclic ring, or

R_{13} and R_{15} are each hydrogen and R_{17}, together with R_{18}, forms a fused fully or partially saturated non-aromatic cyclohexyl ring as defined above, or R_{13}, together with R_{15}, forms a fused fully or partially saturated non-aromatic cyclohexyl ring as defined above, and R_{17} and R_{18} are hydrogen;

-(A)p- and –(A)p*- are optional linkers each independently comprising a straight or branched chain made up of moieties that are the same or different and selected from the group consisting of: –CH_2–, –CHR_3–, –CR_4R_5–, –CH=CH–, –CH=CR_6–, >CR_7-CR_8<, -C=C-, –CR_9=CR_{10}–, -C≡C–, -cycloalkylidene-, -cycloalkenyl-, -arylidene-, -heterocyclo-, carbonyl (-CO-), -O-, -S-, –NH–, –HC=N–, –CR_{11}=N–, –NR_{12}–, –CS–,  ; and p and p* are each individually 0 to 24;

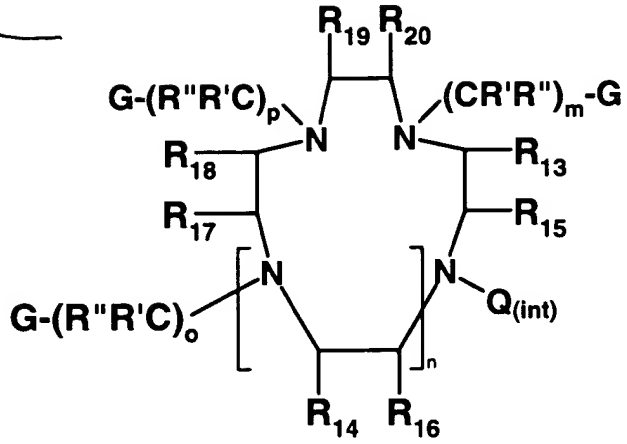
or -X-[(A)p]- or -X-[(A)p*]- in its entirety is the group –Q- as defined above

each -R_3 through -R_5, -R_7 and -R_8 is independently -H, -alkyl, -alkenyl, -alkoxy, -aryl, a 5- or 6-membered nitrogen or oxygen containing heterocycle, halogen, hydroxy or -hydroxyalkyl; and

each -R_1, -R_2, -R_6, -R_9 through -R_{12} is independently -H, -alkyl, -alkoxy, -cycloalkyl, -aryl, -heterocyclo, -hydroxy or -hydroxyalkyl;

or a pharmaceutically acceptable salt thereof;

said intermediate containing at least one free amine, carboxylate or thiocarboxylate functionality that can be used for conjugation to targeting vectors such as folate, said intermediates having the structure of formula **VIa:**



VIa

wherein

n is 0 or 1;

each m, o, and p is independently 1 or 2;

-Q(int) is a conjugatable amine-, carboxylate- or thiocarboxylate-containing group of formula $-[C(R')(R'')]_{s1}-[C(t)(R_{21})]_{s2}-[C(R_{22})(R_{23})]_{s3}-X_3-Y-X_4$;

wherein

s1, s2, s3, and s4 are independently 0 to 2;

X_3 is a single bond, -O-, -S-, -NH- or $-NR_{24}$- if Y is present,

or X_3 is –OH, -SH, $-NH_2$ or–$N(R_{24})H$ if Y and X_4 are absent;

X_4 is a single bond, -OH, -COOH, -SH, $-NHR_{24}$ or $-NH_2$;

Y is a single bond, $-C(R_{25})(R_{26})$-, or Y1

wherein,

Y1 is –C(=X5)-X6-W-, wherein

X_5 is =O or =S;

X_6 is a single bond, -SH, $-NH(R_{38})$, $-NH_2$ or -OH if W and X4 are absent, and is –S-, -O-, -NH-, or $-N(R_{39})$-, if W and X_4 are present;

W is a single bond, or is -alkylidene-, -cycloalkylidene-, -arylidene-, -alkenylidene-, or –alkynylidene-, whose carbon atoms [may or may not be] <u>are optionally</u> substituted;

t is -H, $-R_{27}$, $-C(O)OR_{28}$, $-P(O)(OR_{29}))OH$, $-P(O)(OR_{30}))OR_{31}$, $-P(O)(OR_{32})R_{33}$, $-P(O)(OH)R_{34}$ $-C(O)N(R_{35})(R_{36})$, or $-C(O)NH(R_{37})$;

each -G is independently -C(O)OR'", $-P(O)(OR'")OH$, $-P(O)(OR'")_2$, $-P(O)(OR'")R"$, $-P(O)(OH)R"$ $-C(O)N(R'")_2$, or $-C(O)NH(R'")$;

each -R' and -R" is independently a single bond, -H, -alkyl, -alkoxy, -cycloalkyl, -hydroxyalkyl, -aryl, or -heterocyclo, each of which is optionally substituted,

each -R'" is independently -H, -alkyl, -cycloalkyl, -hydroxyalkyl, -aryl, or -heterocyclo, each of which is optionally substituted,

each $-R_{13}$ through $-R_{23}$, and $-R_{25}$ through $-R_{27}$ is independently -H, -alkyl, alkoxy, -halogen, -hydroxy, -cycloalkyl, -hydroxyalkyl, -aryl, or -heterocyclo, each of which

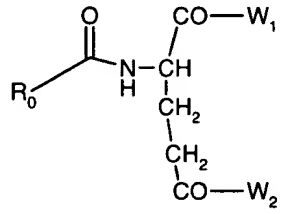
is optionally substituted;

each -R_{24}, and -R_{28} through -R_{39} is independently -H, -alkyl, -alkenyl, cycloalkyl, aryl, a 5- or 6-membered nitrogen or oxygen containing heterocycle, each of which is optionally substituted;

or R_{13} together with R_{15}, and R_{17} together with R_{18}, independently form, together with the carbon atoms in the polyazamacrocycle to which they are attached, a fused fully or partially saturated non-aromatic cyclohexyl ring which [may be unsubstituted or] are optionally substituted by one or more halogen, alkyl, ether, hydroxy, or hydroxyalkyl groups, and which [may be] are optionally further fused to a carbocyclic ring, or R_{13} and R_{15} are each hydrogen and R_{17}, together with R_{18}, forms a fused fully or partially saturated non-aromatic cyclohexyl ring as defined above, or R_{13}, together with R_{15},forms a fused fully or partially saturated non-aromatic cyclohexyl ring as defined above, and R_{17} and R_{18} are hydrogen;

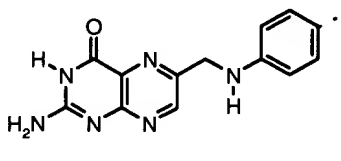
or a pharmaceutically acceptable thereof.--

--29. (Amended) A composition comprising folate-receptor binding ligands and a pharmaceutically acceptable carrier for use in nuclear medicine, magnetic resonance imaging, or neutron capture therapy techniques, said folate-receptor binding ligands comprising dendrimeric first-, second-, third-, and fourth- generation conjugates containing one folate-receptor binding [residue] moiety coupled to one or more macrocyclic metal-chelating ligand radicals that are optionally chelated to paramagnetic, superparamagnetic, radioactive or non-radioactive metals [capable of either being detected] for detection outside the body by imaging means for diagnosis or [capable of] for providing a therapeutic or radiotherapeutic effect; wherein said folate-receptor binding compounds have the structure of formulae **VIIa – VIId:**

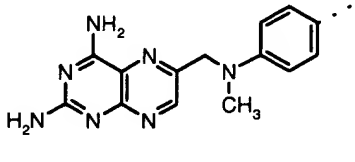


VIIa - VIId

wherein R_0 is a folate-receptor [residue] moiety of formula:



or

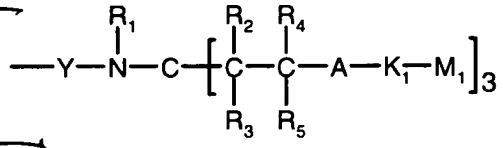


wherein for the first generation dendrimers of formula **VIIa**, bearing one folate-receptor binding [residue] moiety and 3 or 6 metal chelating ligand radicals:

W_1 and W_2 are each independently –OR'", -SR'", -NR'"R'" $-CON(R_2)_2$, -glutamate, -polyglutamate, or $-K_6$;

wherein each -R'" is independently [-H, -alkyl, -aryl,] -cycloalkyl, -hydroxyalkyl, or -heterocyclo;

with the proviso that either W_1, W_2, or both W_1 and W_2 of formula **VIIa** must be $-K_6$, where $-K_6$ is a [residue] moiety of formula **VIIIa**:



VIIIa

wherein

Y is [a single bond or] -Y'-C(=X)–

wherein

X is =O or =S;

Y' is $N(R_6)$-Z-;

wherein

Z is a single bond, -alkylidene-, -vinylidene-, -cycloalkylidene-, or –arylidene-;

A is -C(=O)-, C(=S), or $-CH_2$-$N(R_7)$-;

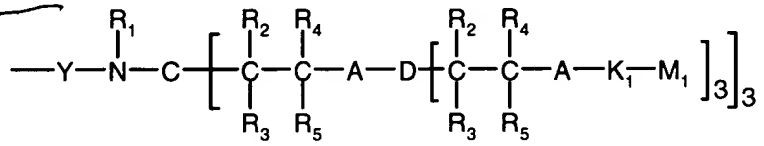
M_1 is a superparamagnetic, paramagnetic, radioactive or non-radioactive metal, and

K_1 is a macrocyclic metal chelating ligand [residue] moiety;

and,

wherein for second generation dendrimers, bearing one folate receptor binding [residue] moiety and 9 or 18 macrocyclic metal-chelating ligand radicals and having the structure of formula **VIIIb**:

W_1 and W_2 are each independently –OR'", -SR'" -NR'"R'", or $-K_7$, wherein each -R'" is independently -H, -alkyl, -aryl, -cycloalkyl, -hydroxyalkyl, or -heterocyclo, and $-K_7$ is a residue of formula **VIIIb**; with the proviso that either W_1, W_2, or both W_1 and W_2 must be $-K_7$



VIIIb

wherein

Y is a single bond or -Y'-C(=X)–

wherein X is =O or =S and Y' is -$N(R_6)$-Z-;

wherein

Z is a single bond, -alkylidene-, -vinylidene-, -cycloalkylidene-, or –

arylidene-;

A is -C(O)-, C(S)-, or $-CH_2-N(R_7)-$;

D is $-N(R_6)-C-$ if A is -C(O)- or –C(S)- or $-C(=X_2)-E-N(R_7)-C-$ if A is $-CH_2-N(R_7)-$;

wherein

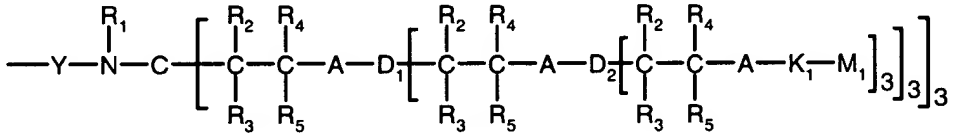
E is a single bond, -alkylidene-, -vinylidene-, -cycloalkylidene-, or –arylidene- and X_2 is =O or =S;

and wherein

for the third generation dendrimeric compounds of formula **VIIc**; bearing one folate receptor binding residue and 27or 54 macrocyclic metal-chelating ligand radicals:

W_1 and W_2 are each independently –OR'", -SR'", -NR'"R'", or $-K_8$ wherein each -R'" is independently -H, -alkyl, -aryl, -cycloalkyl, -hydroxyalkyl, or -heterocyclo, and $-K_8$ is a [residue] moiety of formula **VIIIc**;

with the proviso that either W_1, W_2, or both W_1 and W_2 of the compounds of formula **VIIc** must be $-K_8$:



VIIIc

wherein,

Y is a single bond or -Y'-C(=X)–

wherein

X is =O or =S;

Y' is $-N(R_6)-Z-$;

wherein

Z is a single bond, -alkylidene-, -vinylidene-, -cycloalkylidene-, or –arylidene-;

A is -C(O)-, -C(S)-, or $-CH_2-N(R_7)-$;

D_1 and D_2 are each independently $-N(R_6)-C$ if A is -C(O)- or -C(S)-, and $-C(=X_2)-E-N(R_7)-C$ if A is $-CH_2-N(R_7)-$;

wherein

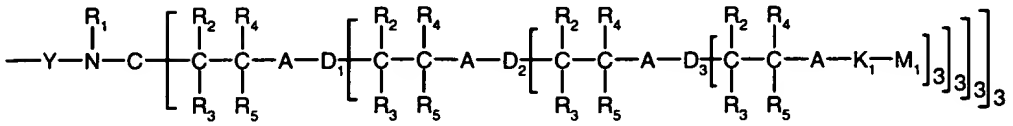
E is a single bond, -alkylidene-, -vinylidene-, -cycloalkylidene-, or –arylidene- and X_2 is =O or =S;

and

wherein for the fourth generation dendrimeric compounds of formula **VIId;** bearing one folate receptor binding [residue] moiety and 81 or 162 macrocyclic metal-chelating ligand radicals:

W_1 and W_2 are each independently –OR'", -SR'", -NR'"R'" or $-K_9$,

wherein each R''' is independently -H, -alkyl, -aryl, -cycloalkyl, -hydroxyalkyl, or -heterocyclo and $-K_9$ is a [residue] moiety of formula **VIIId**; with the proviso that either W_1, W_2, or both W_1 and W_2 of the compounds of formula **VIId** must be $-K_9$):



VIIId

wherein Y is a single bond or -Y'-C(=X)–

wherein

X is =O or =S;

Y' is -N(R_6)-Z-;

wherein

Z is a single bond, -alkylidene-, -vinylidene-, -cycloalkylidene-, or –arylidene-;

A is -C(O)-, -C(S)-, or $-CH_2$-N(R_7)-;

D_1, D_2, and D_3 are each independently –N(R_6)-C if A is -C(O)- or C(S)-, and –C(=X_2)-E-N(R_7)-C if A is $-CH_2$-N(R_7)-;

wherein E is a single bond, -alkylidene-, -vinylidene-, -cycloalkylidene-, or –arylidene- and X_2 is =O or =S; and

each -R_1 to -R_7 of the compounds of formula **VIIIa-VIIId** is independently -H, -alkyl, -hydroxyalkyl, -alkoxy, -alkoxyalkyl, -cycloalkyl, or -aryl; each of which is optionally substituted,

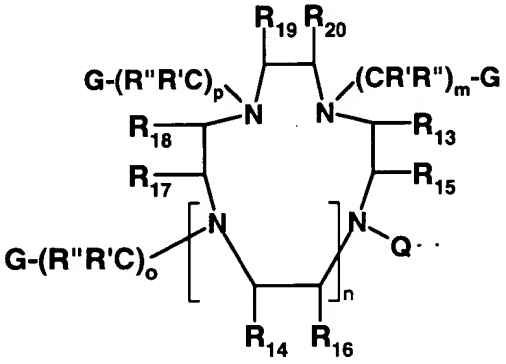
or a pharmaceutically acceptable salt thereof.--

--30. (Amended) The composition of claim 29 wherein W_1 of formula **VIIa – VIId** is a [residue] moiety of formula **VIIIa, VIIIb, VIIIc or VIIId** and W_2 of formula **VIIa – VIId** is –OR''', -SR''', -NR'''R''' -CON(R_2)$_2$, -glutamate, or -polyglutamate, wherein each R''' is independently [-H, -alkyl,] -aryl, -cycloalkyl, [-hydroxyalky], or –heterocyclo.--

--31. (Amended) The composition of claim 29 wherein W_2 of formula **VIIa – VIId** is a [residue] moiety of formula **VIIIa , VIIIb, VIIIc or VIIId**; and W_1 of formula **VIIa – VIId** is –OR''', -SR''', -NR'''R''' -CON(R_2)$_2$, -glutamate, or -polyglutamate, wherein each R''' is independently [-H, -alkyl,] aryl, -cycloalkyl, [hydroxyalkyl,] or –heterocyclo.--

--32. (Amended) The [dendrimeric] composition[s] of claim 29 wherein both W_1 and W_2 of formula **VIIa – VIId** is a [residue] moiety of formula **[VIIIa,] VIIIb, VIIIc or VIIId**].--

--33. (Amended) The [dendrimeric folate-receptor binding] composition[s] of formula **VIIa – VIId** of claim 29 [for use in diagnostic imaging using magnetic resonance or nuclear medicine techniques, or for use in radiation- or neutron-capture therapy,] wherein M_1 is a radioactive-, paramagnetic- or superparamagnetic- metal and each K_1 is a macrocyclic metal chelating ligand radical of formula **VI**:



VI

wherein said metal chelating radical is attached to the remainder of the compound of formulae **VIIa - VIId** via the free –N(R)- atom of the function –Q- if A is –C(O)- or –C(S)- or through the free –C(O)- atom of the function –Q- if A is $-CH_2-N(R_7)-$;

wherein –Q- is $-[C(R')(R'')]_{s1}-[C(t)(R_{21})]_{s2}--[C(R_{22})(R_{23})]_{s3}-X3-Y-X4-$;

wherein

s1, s2, s3, and s4 are independently 0 to 2;

X3, X4, X5, and X6 are independently a single bond, –O-, -S-, or $-N(R_{24})-$;

Y is a single bond, $-C(R_{25})(R_{26})-$, or Y1,

wherein Y1 is –C(=X5)-X6-W-,

wherein

W is a single bond, -alkylidene-, -cycloalkylidene-, -arylidene-, -alkenylidene-, or –alkynylidene-, whose carbon atoms [may or may not be] are optionally substituted;

t is H, R_{27}, $-C(O)OR_{28}$, $-P(O)(OR_{29}))OH$, $-P(O)(OR_{30}))OR_{31}$, $-P(O)(OR_{32})R_{33}$, $-P(O)(OH)R_{34}$, $-C(O)N(R_{35})(R_{36})$, or $C(O)NH(R_{37})$;

each G is independently -C(O)OR'", -P(O)(OR'")OH, $-P(O)(OR'")_2$, -P(O)(OR'")R", -P(O)(OH)R" $C(O)N(R'")_2$, or C(O)NH(R'");

each R' and R" is independently a single bond, -H, -alkyl, -alkoxy, -cycloalkyl, -

hydroxyalkyl, -aryl, or -heterocyclo, each of which is optionally substituted,

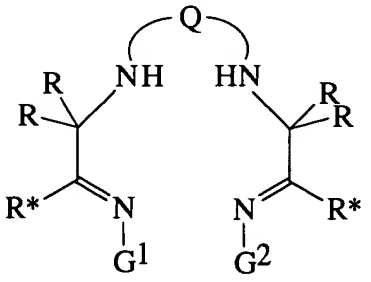
each R'" is independently -H, -alkyl, -cycloalkyl, -hydroxyalkyl, -aryl, or -heterocyclo, each of which is optionally substituted,

each $-R_{13}$ through $-R_{23}$, and $-R_{25}$ through $-R_{27}$ is independently -H, -alkyl, -alkoxy, -halogen, -hydroxy, -cycloalkyl, -hydroxyalkyl, -aryl, or -heterocyclo, each of which is optionally substituted;

each $-R_{24}$, and $-R_{28}$ through $-R_{37}$ is independently -H, -alkyl, -alkenyl, -cycloalkyl, -aryl, or a 5- or 6-membered nitrogen or oxygen containing heterocycle, each of which is optionally substituted;

or a pharmaceutically accepted salt thereof.--

--34. (Amended) The [dendrimeric folate receptor binding] composition of formula **VIIa – VIId** of claim 29 wherein M_1 is a radioactive metal and at least one $-K_1$ is a macrocyclic metal chelating ligand radical of formula **V**:



V

wherein

-Q- is the group $-(C(RR))_{m1}-(Y^1)_n-(C(RR))_{m2}-(Y^2-(C(RR))_{m3})_{n1}$;

Y^1 and Y^2 are each independently $-CH_2-$, -NR-, -O-, -S-, -SO-, $-SO_2-$ or -Se-;

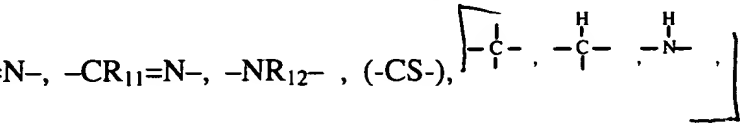
n and n1 are each independently 0 or 1; and m1, m2 and m3 are independently 0 or an integer from 1 to 4; provided that m1 and m2 are not both 0, that m1 + m2 + n +n1 is less than 6 and that a carbon atom bearing an R group is not directly bonded to more than one heteroatom;

each -R and -R* group is independently: $-R^4$; -alkoxy; -hydroxy; -halogen, especially fluoro, -haloalkyl, $-OR^5$, $-C(O)-R^5$, $-C(O)-N(R^5)_2$, $-N(R^5)_2$, $-N(R^5)-COR^5$, -alkyl-$C(O)-OR^5$, -alkyl-$C(O)-N(R^5)_2$, -alkyl-$N(R^5)_2$-, -alkyl-$N(R^5)-COR^5$, -aryl-$C(O)-OR^5$, -aryl-$C(O)-N(R^5)_2$, aryl-$N(R^5)_2$-, -aryl-$N(R^5)-COR^5$, -nitrile, -acyl, -acyloxy, -heterocyclo, -hydroxyalkyl, -alkoxyalkyl; -hydroxyaryl, arylalkyl, $-SO_2-R^5$, -alkyl-SO_2-R^5, or $-[R^3]-$;

wherein

$-[R^3]-$ is a linking group $-[(A)p]-$ that links the metal chelating ligand radical of formula **V** to the remainder of the molecule of formulae **VIIa** through **VIId**;

wherein $-[(A)p]-$ comprises a straight or branched chain of individual moieties that are the same or different and selected from the group consisting of: $-CH_2-$, $-CHR_3-$, $-CR_4R_5-$, -CH=CH–, $-CH=CR_6-$,

$>CR_7\text{-}CR_8<$, -C=C-, $-CR_9=CR_{10}-$, -C≡C-, -cycloalkylidene-, -cycloalkenyl-, -arylidene-, -heterocyclo-, carbonyl (-CO-), -O-, -S-, -NH-, $-HC=N-$, $-CR_{11}=N-$, $-NR_{12}-$, (-CS-),  and

p is an integer from 0 to 24;

each $-R^4$ and $-R_3$ through $-R_5$ is independently -H, -alkyl, -alkoxy, -hydroxy, -cycloalkyl, -hydroxyalkyl, -aryl, or -heterocyclo, each of which is optionally substituted;

each $-R^5$ and R_6 through R_{12} is independently -H, -alkyl, -aryl, -cycloalkyl or -hydroxyalkyl, each of which is independently substituted; or

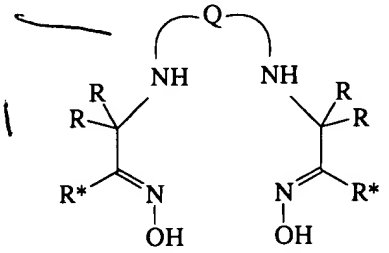
two R groups, or an R group and an R* group, taken together with the one or more atoms to which they are bonded, form a saturated or unsaturated, spiro or fused, carbocyclic [(such as fused 1,2-phenyl)] or heterocyclic ring which [may be unsubstituted] is optionally substituted by one or more [groups] R or R* groups [above];

each $-G^1$ and $-G^2$ is independently -OH or $-(NR^6)_2$; with the proviso that at least one of $-G^1$ or $-G^2$ is $-(NR^6)_2$, and each $-R^6$ is independently -hydrogen, -alkyl, -aryl, -acyl or $-[R^3]-$;

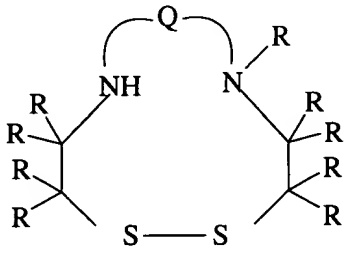
with the proviso that at least one -R , -R*, or $-R^6$ group is $-[R^3]-$;

or a pharmaceutically acceptable salt thereof.--

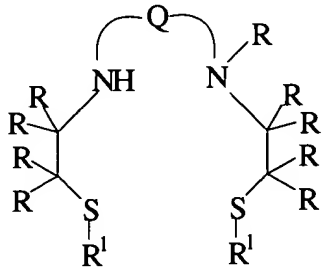
--35. (Amended) The [dendrimeric folate-receptor binding] composition of formula **VIIa – VIId** of claim 29 [for use in nuclear medicine or radiotherapy] wherein M_1 is a radioactive isotope and at least one K_1 is a macrocyclic metal chelating ligand of formula **IIIa - IIIc**:



IIIa



IIIb



IIIc

wherein

Q is the group $-(C(RR))_{m1}\text{-}Y^1(C(RR))_{m2}\text{-}(Y^2\text{-}(C(RR))_{m3})_n-$,

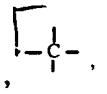
wherein

Y^1 and Y^2 are independently $-CH_2-$, -NR-, -O-, -S-, -SO-, $-SO_2-$ or -Se-;

n is 0 or 1; and m1, m2 and m3 are integers [independently selected] from 0 to 4, provided that the sum of m1 and m2 is greater than zero;

all R and R* groups are independently $-R^4$, -Cl, -F, -Br, $-OR^5$, $-COOR^5$, $-CON(R^5)_2$, $-N(R^5)_2$, -alkyl-$COOR^5$, -alkyl-$C(O)$-$N(R^5)_2$, -alkyl-$N(R^5)_2$, $-C(O)OR^5$, $-C(O)N(R^5)_2$, -aryl-$N(R^5)_2$, -acyl, -acyloxy, -heterocyclo, -hydroxyalkyl, $-SO_2-R^5$, -alkyl-SO_2-R^5, or $-[R^3]-$;

wherein

$-[R^3]-$ is a linking group $-[(A)p]-$ that links the metal chelating ligand of formula **IIIa, IIIb, or IIIc** to the remainder of the molecule; wherein $-[(A)p]-$ comprises a straight or branched chain of individual moieties that are the same or different and selected from the group consisting of: $-CH_2-$, $-CHR_3-$, $-CR_4R_5-$, -CH=CH-, $-CH=CR_6-$, $>CR_7-CR_8<$, -C=C-, $-CR_9=CR_{10}-$, -C≡C-, -cycloalkylidene-, -cycloalkenyl-, -arylidene-, -heterocyclo-, carbonyl -(CO)-, -O-, -S-, -NH-, $-HC=N-$, $-CR_{11}=N-$, $-NR_{12}-$, -(CS)-,  , and

p is an integer from 0 to 24;

each $-R^4$ and $-R_3$ through $-R_5$ is independently -H, -alkyl, -alkoxy, -hydroxy, -cycloalkyl, -hydroxyalkyl, -aryl, or -heterocyclo, each of which is optionally substituted;

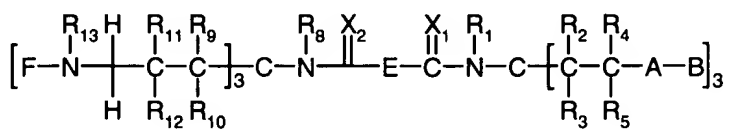
each $-R^5$ and $-R_6$ through R_{12} is independently -H, -alkyl, -aryl, -cycloalkyl or -hydroxyalkyl, each of which is independently substituted;

with the provisos that a carbon atom bearing an -R group is not directly bonded to more than one heteroatom; and that at least one -R or -R* group on $-K_1$ is $-[R^3]-$

or a pharmaceutically acceptable salt thereof.--

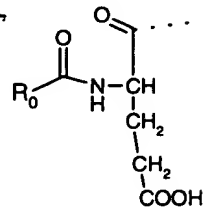
--~~36~~ 13. (Amended) A folate-receptor binding ligand comprising dendrimeric first-, second-, third-, and fourth- generation conjugates containing one or more folate-receptor binding [residues] moieties coupled to one or more macrocyclic metal-chelating ligand radicals [that are capable of either being detected] for detection outside the body by imaging means for diagnosis or [capable of] for providing a therapeutic or radiotherapeutic effect, wherein said folate-receptor binding ligands have the structure of formulae **IXa, IXb, IXc,** and **IXd,** representing dendrimers of generations 1, 2, 3, and 4, respectively,

wherein for the first generation dendrimers of formula **IXa**, bearing three folate and three metal chelating ligand radicals;

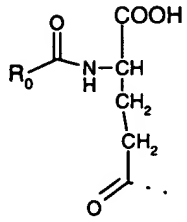


IXa

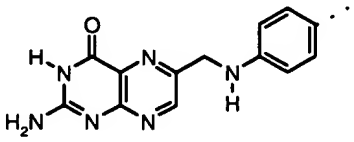
F is a folate-receptor binding [residue] moiety of formula:



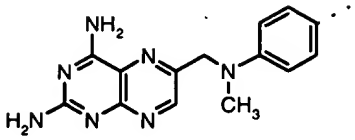
or



wherein R_0 is a [residue] moiety of formula:

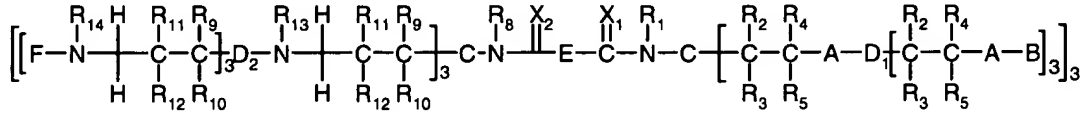


or



each X_1 through X_4 is independently =O or =S;
each A is -C(O)-, -C(S)-, or $-CH_2-N(R_7)-$;
E is a single bond, -alkylidene-, -vinylidene-, -cycloalkylidene-, or –arylidene-;
B is a macrocyclic metal-chelating ligand radical that is attached to A via an amide or thioamide bond and is optionally chelated to a paramagnetic, superparamagnetic, radioactive or non-radioactive metal;
$-R_1$, $-R_6$ through $-R_8$, $-R_{13}$, and $-R_{14}$ are independently -H, -alkyl, -hydroxyalkyl, -cycloalkyl, or -aryl;
$-R_2$ through $-R_5$ and $-R_9$ through $-R_{12}$ are independently -H, -alkyl, -hydroxyalkyl, -alkoxy, -hydroxyalkyl, -halogen, -cycloalkyl, -aryl or -heterocyclo;
or a pharmaceutically accepted salt thereof;

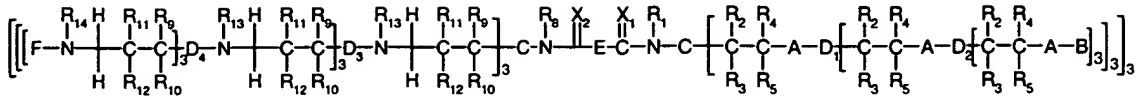
and wherein for the second generation dendrimeric compounds of formula **IXb**, bearing nine folate-receptor binding [residue] moieties and nine metal-chelating ligand radicals:



IXb

A, B, E, F, X_1 through X_4 and all -R groups are as defined for the compounds of formula **IXa**;
D_1 and D_2 are independently $-N(R_6)-C$ if A is -C(O)- or –C(S)-, and $-C(=X_3)-E-N(R_7)-C$ if A is $-CH_2-N(R_7)-$;

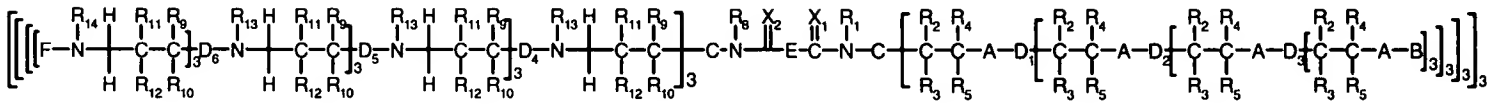
and wherein for the third generation dendrimeric compounds of formula **IXc**, bearing 27 folate receptor binding [residue] moieties and 27 metal chelating ligand radicals:



IXc

D_1, D_2, D_3, and D_4 are independently $-N(R_6)-C$ if A is -C(O)- or –C(S)-, and $-C(=X_3)-E-N(R_7)-C$ if A is $-CH_2-N(R_7)-$; and all other groups are defined as above;

and wherein for the fourth generation dendrimeric compounds of formula **IXd**, bearing 81 folate receptor binding [residue] moieties to 81 metal chelating ligands:

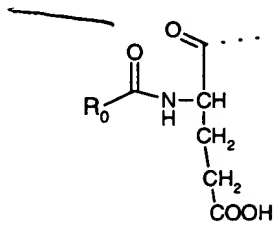


IXd

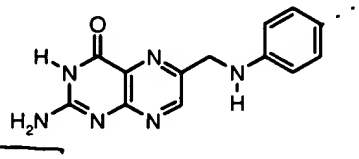
D_1, D_2, D_3, D_4, D_5, and D_6 are each independently $-N(R_6)-C$ if A is -C(O)- or -C(S)-, and $-C(=X_3)-E-N(R7)-C$ if A is $-CH_2-N(R_7)-$;

or a pharmaceutically acceptable salt thereof.--

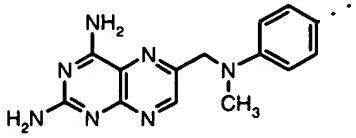
~~37~~. (Amended) The [dendrimeric composition] folate-receptor binding ligand of claim ~~36~~ wherein F of formulae **[IXa,] IXb, IXc,** and **IXd** is a folate-receptor binding [residue] moiety of formula:



wherein R_0 is a [residue] moiety of formula:

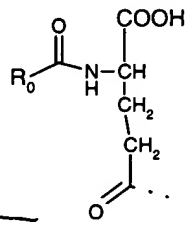


or

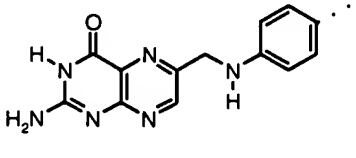


or a pharmaceutically acceptable salt thereof.--

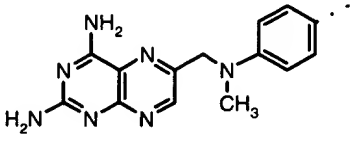
~~38~~. (Amended) The [dendrimeric] folate-receptor binding ligand [composition] of claim ~~36~~ wherein F of formulae **[IXa,] IXb, IXc,** and **IXd** is a folate receptor binding [residue] moiety of formula:



wherein R_0 is a [residue] moiety of formula:



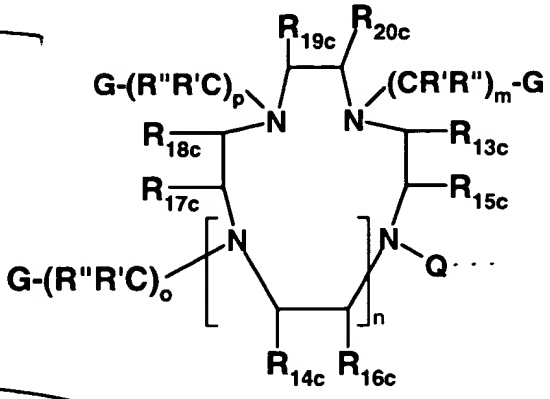
or



or a pharmaceutically acceptable salt thereof.--

~~39~~. (Amended) The folate-receptor binding ligand [composition] of formulae **[IXa,] IXb, IXc,** and **IXd** of claim ~~36~~, wherein B is a polyaza macrocyclic ligand radical of

formula **VIc** that is optionally chelated to a paramagnetic, superparamagnetic, radioactive or non-radioactive metal,



VIc

wherein said macrocyclic ligand radical is attached to A via an amide or thioamide linkage [through a free N atom of the function –Q- if A is –C(O)- or –C(S)- or] through a free –C(O)- group of the function –Q- if A is $-CH_2-N(R_7)-$;

–Q- is $-[C(R')(R'')]_{s1}-[C(t)(R_{21})]_{s2}-[C(R_{22})(R_{23})]_{s3}-X_3-Y-X_4-$;

wherein

s1, s2, s3, and s4 are independently 0 to 2;

$-X_3$, $-X_4$, $-X_5$, and $-X_6$ are independently a single bond, –O-, -S-, or $-N(R_{24})-$;

Y is a single bond, $-C(R_{25})(R_{26})-$, or Y1,

wherein Y1 is $-C(=X_5)-X_6-W-$,

wherein

W is a single bond, -alkylidene-, -cycloalkylidene-, -arylidene-, -alkenylidene-, or –alkynylidene-, whose carbon atoms [may or may not be] are optionally substituted;

t is H, R_{27}, $-C(O)OR_{28}$, $-P(O)(OR_{29}))OH$, $-P(O)(OR_{30}))OR_{31}$, $-P(O)(OR_{32})R_{33}$, $-P(O)(OH)R_{34}$, $-C(O)N(R_{35})(R_{36})$, or $C(O)NH(R_{37})$;

each G is independently -C(O)OR'", -P(O)(OR'")OH, $-P(O)(OR'")_2$, -P(O)(OR'")R", -P(O)(OH)R" $-C(O)N(R'")_2$, or -C(O)NH(R'");

each -R' and -R" is independently a single bond, -H, -alkyl, -alkoxy, -cycloalkyl, -hydroxyalkyl, -aryl, or -heterocyclo, each of which is optionally substituted,

each -R'" is independently -H, -alkyl, -cycloalkyl, -hydroxyalkyl, -aryl, or -heterocyclo, each of which is optionally substituted,

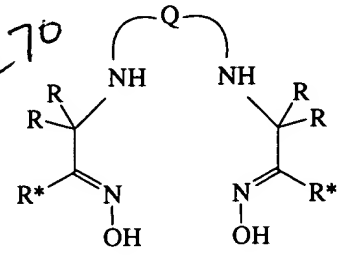
each $-R_{13c}$ through $-R_{20c}$, $-R_{21}$ through $-R_{23}$, and $-R_{25}$ through $-R_{27}$ is independently -H, -alkyl, -alkoxy, -halogen, -hydroxy, -cycloalkyl, -hydroxyalkyl, -aryl, or -heterocyclo, each of which is optionally substituted;

each $-R_{24}$, and $-R_{28}$ through $-R_{37}$ is independently -H, -alkyl, -alkenyl, -cycloalkyl, -aryl, a 5- or 6-membered nitrogen or

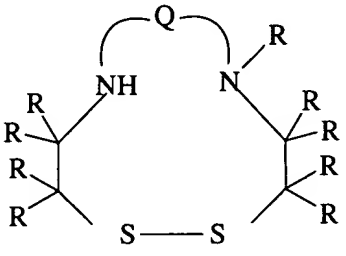
oxygen-containing heterocycle, each of which is optionally substituted;

or a pharmaceutically accepted salt thereof.--

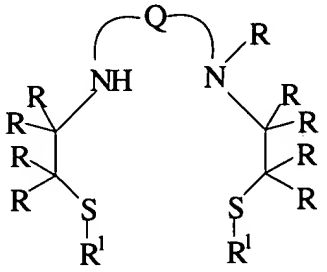
--40. (Amended) The [dendrimeric] folate-receptor binding ligand [composition] of formulae **IXa, IXb, IXc,** and **IXd** of claim 36 wherein B is a metal-chelating ligand radical of formula **IIIa - IIIc** that is optionally chelated to a paramagnetic, superparamagnetic, radioactive or non-radioactive metal:



IIIa



IIIb



IIIc

wherein

Q is the group $-(C(RR))_{m1}-Y^1(C(RR))_{m2}-(Y^2-(C(RR))_{m3})_n-$,

wherein

Y^1 and Y^2 are independently $-CH_2-$, -NR-, -O-, -S-, -SO-, $-SO_2-$ or -Se-;

n is 0 or 1; and m1, m2 and m3 are integers [independently selected] from 0 to 4, provided that the sum of m1 and m2 is greater than zero;

all R and R* groups are independently $-R^4$, -Cl, -F, -Br, $-OR^5$, $-COOR^5$, $-CON(R^5)_2$, $-N(R^5)_2$, -alkyl-$COOR^5$, -alkyl-$C(O)-N(R^5)_2$, -alkyl-$N(R^5)_2$, $-C(O)OR^5$, $-C(O)N(R^5)_2$, -aryl-$N(R^5)_2$, acyl, acyloxy, heterocyclo, hydroxyalkyl, $-SO_2-R^5$, -alkyl-SO_2-R^5, or $-[R^3]-$;

wherein $-[R^3]-$ is a linking group $-[(A)p]-$ that couples the metal chelating radical of formula **IIIa, IIIb,** or **IIIc** to the remainder of the molecule;

$-[(A)p]-$ comprises a straight or branched chain of individual moieties that are the same or different and selected from the group consisting of: $-CH_2-$, $-CHR_3-$, $-CR_4R_5-$, -CH=CH-, $-CH=CR_6-$, $>CR_7-CR_8<$, -C=C-, $-CR_9=CR_{10}-$, -C≡C-, -cycloalkylidene-, -cycloalkenyl-, -arylidene-, -heterocyclo-, carbonyl -(CO)-, -O-, -S-, -NH-, $-HC=N-$, $-CR_{11}=N-$, $-NR_{12}-$, -CS-, and  and

p is an integer from 0 to 24;

each $-R^4$ and $-R_3$ through $-R_5$ is independently -H, -alkyl, -alkoxy, -hydroxy, -cycloalkyl, -hydroxyalkyl, -aryl, or -heterocyclo, each of

which is optionally substituted;

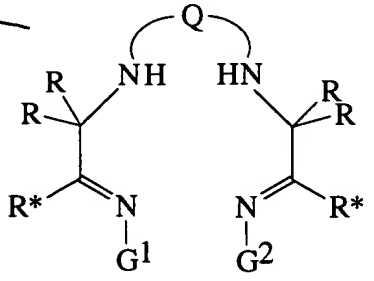
each -R^5 and -R_6 through -R_{12} is independently -H, -alkyl, -aryl, -cycloalkyl or -hydroxyalkyl, each of which is independently substituted;

[and all other groups are defined as in claim 35,]

with the provisos that a carbon atom bearing an -R group is not directly bonded to more than one heteroatom; and that at least one -R or -R* group on the metal chelating radical -K_1 of formulae **IIIa, IIIb,** or **IIIc** is -[R^3]-;

or a pharmaceutically acceptable salt thereof.--

--41. (Amended) The [dendrimeric] folate-receptor binding ligand [composition] of formulae **IXa, IXb, IXc,** and **IXd** of claim 36, wherein B is a metal-chelating ligand radical of formula **V** that is optionally chelated to a paramagnetic, superparamagnetic, radioactive or non-radioactive metal:



V

wherein

-Q- is the group -$(C(RR))_{m1}$-$(Y^1)_n$ -$(C(RR))_{m2}$ -$(Y^2$-$(C(RR))_{m3})_{n1}$;

Y^1 and Y^2 are each independently -CH_2-, -NR-, -O-, -S-, -SO-, -SO_2- or -Se-;

n and n1 are each independently 0 or 1; and m1, m2 and m3 are [independently] 0 or an integer from 1 to 4; provided that m1 and m2 are not both 0, that m1 + m2 + n +n1 is less than 6 and that a carbon atom bearing an R group is not directly bonded to more than one heteroatom;

each -R and -R* group is independently: -R^4; -alkoxy; -hydroxy; -halogen, [especially fluoro,] -haloalkyl, -OR^5, -C(O)-R^5, -C(O)-N(R^5)2, -N(R^5)2, -N(R^5)-COR^5, -alkyl-C(O)-OR^5, -alkyl-C(O)-N(R^5)2, -alkyl-N(R^5)2-, -alkyl-N(R^5)-COR^5, -aryl-C(O)-OR^5, -aryl-C(O)-N(R^5)2, aryl-N(R^5)2-, -aryl-N(R^5)-COR^5, -nitrile, -acyl, -acyloxy, -heterocyclo, -hydroxyalkyl, -alkoxyalkyl, -hydroxyaryl, arylalkyl, -SO_2-R^5, -alkyl-SO_2-R^5, or –[R^3]- ;

wherein

-[R^3]- is a linking group –[(A)p]- that links the metal chelating ligand radical of formula **V** to the remainder of the molecule of formulae **IXa, IXb, IXc,** and **IXd**;

wherein –[(A)p]- comprises a straight or branched chain of individual moieties that are the same or different and are selected from the group

T1 1281

consisting of: $-CH_2-$, $-CHR_3-$, $-CR_4R_5-$, $-CH=CH-$, $-CH=CR_6-$, $>CR_7-CR_8<$, -C=C-, $-CR_9=CR_{10}-$, -C≡C-, -cycloalkylidene-, -cycloalkenyl-, -arylidene-, -heterocyclo-, carbonyl (-CO-), -O-, -S-, -NH-, $-HC=N-$, $-CR_{11}=N-$, $-NR_{12}-$, -CS-), [$-\overset{|}{\underset{|}{C}}-$, $-\overset{H}{\overset{|}{\underset{|}{C}}}-$, $-\overset{H}{\overset{|}{N}}-$] and

cont A4

p is an integer from 0 to 24;

each $-R^4$ and $-R_3$ through $-R_5$ is independently -H, -alkyl, -alkoxy, -hydroxy, -cycloalkyl, -hydroxyalkyl, -aryl, or -heterocyclo, each of which is optionally substituted;

each $-R^5$ and $-R_6$ through $-R_{12}$ is independently -H, -alkyl, -aryl, -cycloalkyl or -hydroxyalkyl, each of which is independently substituted; or

two R groups, or an R group and an R* group, taken together with the one or more atoms to which they are bonded, form a saturated or unsaturated, spiro or fused, carbocyclic [(such as fused 1,2-phenyl)] or heterocyclic ring which may be unsubstituted or substituted by one or more groups of R or R* [groups above];

each $-G^1$ and $-G^2$ is independently -OH or $-(NR^6)_2$; with the proviso that at least one of $-G^1$ or $-G^2$ is $-(NR^6)_2$, and each $-R^6$ is independently -hydrogen, -alkyl, -aryl, -acyl or $-[R^3]-$;

[and all other groups are defined as in claim **80,**]

with the provisos that a carbon atom bearing an -R group is not directly bonded to more than one heteroatom and that at least one -R , -R*, or $-R^6$ group on the metal chelating radical $-K_1$ of formula **V** is $-[R^3]-$;

or a pharmaceutically acceptable salt thereof.--

--~~81~~ 19. (Amended) The [A diagnostic or radiotherapeutic] composition of claim ~~29~~ 6 wherein W_1, W_2 or both W_1 and W_2 contain metal chelating ligands of formula **V** that are chelated to a radioactive metal[,]:

A5

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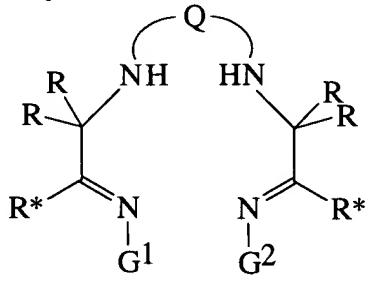


V

wherein

Q is the group $-(C(RR))_{m1}-(Y^1)_n-(C(RR))_{m2}-(Y^2-(C(RR))_{m3})_{n1}$;

Y^1 and Y^2 are each independently $-CH_2-$, -NR-, -O-, -S-, -SO-, $-SO_2-$ or -Se-;

n and n1 are each independently 0 or 1; and m1, m2 and m3 are independently 0 or an integer from 1 to 4; provided that m1 and m2 are not both 0, that m1 + m2 + n +n1 is less than 6 and that a carbon atom bearing an R group is not directly bonded to more than one heteroatom;

each R and R* group is independently: -H, $-R^4$; -alkoxy; -hydroxy; -halogen, especially fluoro, -haloalkyl, $-OR^5$, $-C(O)-R^5$, $-C(O)-N(R^5)_2$, $-N(R^5)_2$, $-N(R^5)-COR^5$, $-alkyl-C(O)-OR^5$, $-alkyl-C(O)-N(R^5)_2$, $-alkyl-N(R^5)_2-$, $-alkyl-N(R^5)-COR^5$, $-aryl-C(O)-OR^5$, $-aryl-C(O)-N(R^5)_2$, $aryl-N(R^5)_2-$, $-aryl-N(R^5)-COR^5$, -nitrile, -acyl, -acyloxy, -heterocyclo, -hydroxyalkyl, -alkoxyalkyl, -hydroxyaryl, -arylalkyl, $-SO_2-R^5$, $-alkyl-SO_2-R^5$, or $-[R^3]-$;

wherein

each $-[R^3]-$ is, in its entirety, the linking group $-[(A)p^*]-$ that serves to couple the metal chelating ligand radical $-K_5$ to –X-;

each $-R^4$ is independently -H, -alkyl, -alkoxy, -hydroxy, -cycloalkyl, -hydroxyalkyl, -aryl, or -heterocyclo, each of which is optionally substituted;

each $-R^5$ is independently -H, -alkyl, -aryl, -cycloalkyl or -hydroxyalkyl, each of which is independently substituted;

or

two R groups, or an R group and an R* group, taken together with the one or more atoms to which they are bonded, form a saturated or unsaturated, spiro or fused, carbocyclic (such as fused 1,2-phenyl) or heterocyclic ring which may be unsubstituted or substituted by one or more groups R or R* groups above;

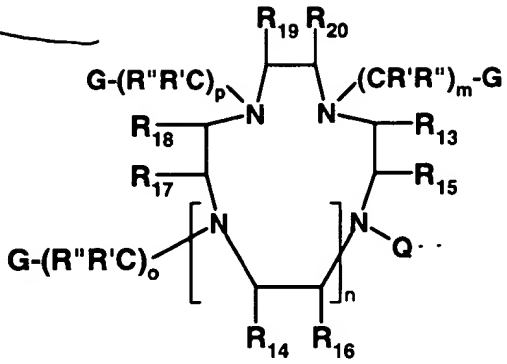
each $-G^1$ and $-G^2$ is independently -OH or $-(NR^6)_2$; with the proviso that at least one of $-G^1$ or $-G^2$ is $-(NR^6)_2$, where each $-R^6$ is independently -hydrogen, -alkyl, -aryl, -acyl or $-[R^3]-$; and

A is a linking group; and p is 0 or a positive integer;

with the proviso that at one to three -R , -R*, or $-R^6$ groups is $-[R^3]-$;

or a pharmaceutically acceptable salt thereof.--

--82. (Amended) The [diagnostic] composition of claim 29 wherein W_1, W_2 or both W_1 and W_2 contain metal chelating ligands of formula **V** that are chelated to a radioactive metal[,]:



VI

wherein

n is 0 [or 1];

each m, o, and p is independently 1 or 2;

Q is $-[C(R')(R'')]_{s1}-[C(t)(R_{21})]_{s2}-[C(R_{22})(R_{23})]_{s3}$-X3-Y-X4-;

wherein

s1, s2, s3, and s4 are independently 0 to 2;

X3, X4, X5 and X6 are independently a single bond, -O-, -S-, or -$N(R_{24})$-;

Y is a [single bond,] $-C(R_{25})(R_{26})$-, or Y1

wherein Y1 is –C(=X5)-X6-W-,

wherein W is a single bond, -alkylidene-, -cycloalkylidene-, -arylidene-, -alkenylidene-, or –alkynylidene-, whose carbon atoms may or may not be substituted;

t is H, R_{27}, $-C(O)OR_{28}$, $-P(O)(OR_{29}))OH$, $-P(O)(OR_{30}))OR_{31}$, $-P(O)(OR_{32})R_{33}$, $-P(O)(OH)R_{34}$ $-C(O)N(R_{35})(R_{36})$, or $C(O)NH(R_{37})$;

each G is independently -C(O)OR'", -P(O)(OR'")OH, -P(O)(OR'")2, -P(O)(OR'")R", -P(O)(OH)R" C(O)N(R'")2, or C(O)NH(R'");

each -R' and -R" is independently a single bond, -H, -alkyl, -alkoxy, -cycloalkyl, hydroxyalkyl, -aryl, or -heterocyclo, each of which is optionally substituted,

each -R'" is independently a -H, -alkyl, -cycloalkyl, -hydroxyalkyl, -aryl, or -heterocyclo, each of which is optionally substituted,

each $-R_{13}$ through $-R_{23}$, and $-R_{24}$, through $-R_{27}$ is independently -H, -alkyl, -alkoxy, -halogen, -hydroxy, -cycloalkyl, -hydroxyalkyl, aryl, or -heterocyclo, each of which is optionally substituted;

each $-R_{24}$, and $-R_{28}$ through $-R_{37}$ is independently -H, -alkyl, -alkenyl, -cycloalkyl, -aryl, a 5- or 6-membered nitrogen or oxygen containing heterocycle, each of which is optionally substituted;

or R_{13} together with R_{15}, and R_{17} together with R_{18}, independently form, together with the carbon atoms in the poly-aza macrocycle to which they are attached, a fused fully or partially saturated non-aromatic cyclohexyl ring which may be